PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 23 January 2001 (23.01.01)	
International application No. PCT/US00/07277	**Applicant's or agent's file reference** PF-0683 PCT
International filing date (day/month/year) 17 March 2000 (17.03.00)	**Priority date** (day/month/year) 18 March 1999 (18.03.99)
Applicant BANDMAN, Olga et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

06 October 2000 (06.10.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Kiwa Mpay
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

09193706-0

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
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(43) International Publication Date
21 September 2000 (21.09.2000)

PCT

(10) International Publication Number
WO 00/55332 A3

(51) International Patent Classification[7]: C12N 15/54, 15/55, 9/12, 9/16, C07K 16/18, 16/40, C12Q 1/68, A61K 38/45, 38/46

(21) International Application Number: PCT/US00/07277

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60/125,593	18 March 1999 (18.03.1999)	US
60/135,049	20 May 1999 (20.05.1999)	US
60/143,188	9 July 1999 (09.07.1999)	US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier applications:

US	60/135,049 (CIP)
Filed on	20 May 1999 (20.05.1999)
US	60/143,188 (CIP)
Filed on	9 July 1999 (09.07.1999)
US	60/125,593 (CIP)
Filed on	18 March 1999 (18.03.1999)

(71) Applicant *(for all designated States except US)*: **INCYTE PHARMACEUTICALS, INC.** [US/US]; 3160 Porter Drive, Palo Alto, CA 94304 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **BANDMAN, Olga** [US/US]; 366 Anna Avenue, Moutain View, CA 94043 (US). **TANG, Y., Tom** [CN/US]; 4230 Ranwick Court, San Jose, CA 95118 (US). **YUE, Henry** [US/US]; 826 Lois Avenue, Sunnyvale, CA 94087 (US). **HILLMAN, Jennifer, L.** [US/US]; 230 Monroe Drive, #12, Mountain View, CA 94040 (US). **BAUGHN, Mariah, R.** [US/US]; 14244 Santiago Road, Sunnyvale, CA 94577 (US). **AZIMZAI, Yalda** [US/US]; 2045 Rock Springs Drive, Hayward, CA 94545 (US). **LU, Dyung, Aina, M.** [US/US]; 55 Park Belmont Place, San Jose, CA 95136 (US). **AU-YOUNG, Janice** [US/US]; 233 Golden Eagle Lane, Brisbane, CA 94005 (US).

(74) Agents: **HAMLET-COX, Diana** et al.; Incyte Pharmaceuticals, Inc., 3160 Porter Drive, Palo Alto, CA 94304 (US).

(81) Designated States *(national)*: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
10 January 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/55332 A3

(54) Title: HUMAN REGULATORS OF INTRACELLULAR PHOSPHORYLATION

(57) Abstract: The invention provides human regulators of intracellular phosphorylation (HRIP) and polynucleotides which identify and encode HRIP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of HRIP.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/07277

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/54 C12N15/55 C12N9/12 C12N9/16 C07K16/18
C07K16/40 C12Q1/68 A61K38/45 A61K38/46

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K C12Q A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 39446 A (HUMAN GENOME SCIENCES, INC.) 11 September 1998 (1998-09-11) abstract page 1, line 1 -page 2, line 8 page 62, line 6 - line 29 page 87, line 10 -page 93, line 25 page 98, line 1 -page 101, line 6 page 365 -page 366 page 381; claims 1,3 -& GCG_GENESEQ_D database, accession number V59579 6 January 1999 "Human secreted protein gene 69 clone HETGJ09" XP002149750 the whole document --- -/--	10-14

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 October 2000	11. JAN 2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fuchs, U

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/07277

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	TANOUE, T. ET AL.: "Molecular Cloning and Characterziation of a Novel Dual Specificity Phosphatase, MKP-5" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 28, 9 July 1999 (1999-07-09), pages 19949-19956, XP002148678 the whole document	1-3,5,6, 8-14
A	GROOM, L.A. ET AL.: "Differential regulation of the MAP, SAP and RK/p38 kinases by Pyst1, a novel cytosolic dual-specific phosphatase" EMBO JOURNAL, vol. 15, no. 14, 15 July 1996 (1996-07-15), pages 3621-3632, XP000925967 the whole document	1-17,20, 23
A	WO 99 01541 A (TULARIK INC.) 14 January 1999 (1999-01-14) abstract page 4, line 10 -page 16, line 13 page 17 -page 18; claims 1-11	1-17,20, 23
A	WO 99 00507 A (INCYTE PHARMACEUTICALS, INC.) 7 January 1999 (1999-01-07) abstract page 2, line 13 -page 3, line 31 page 38, line 10 -page 46, line 10 page 55 -page 57; claims 1-21	1-17,20, 23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/07277

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 16 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: 18, 19, 21 and 22
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-17, 20, 23 partially

Remark n Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-17, 20, 23 partially

Invention 1

An isolated polypetide comprising an amino acid sequence selected from the group consisting of: a) an amino acid sequence having the SEQ ID NO: 1, b) a naturally occurring amino acid sequence having at least 90% sequence identity to SEQ ID NO: 1, c) a biologically active fragment of SEQ ID NO: 1, d) an immunogenic fragment of SEQ ID NO: 1; an isolated polynucleotide encoding said polypeptide; a recombinant polynucleotide comprising said polynucleotide; a cell transformed with said recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; a method for producing said polypeptide; an isolated antibody which specifically binds to said polypeptide; an isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of: a) a polynucleotide sequence having the SEQ ID NO: 15, b) a naturally occurring polynucleotide sequence having at least 90% sequence identity to SEQ ID NO: 15, c) a polynucleotide sequence complementary to a); d) a polynucleotide sequence complementary to b); an RNA equivalent of a)-d); a method for detecting a target polynucleotide in a sample having the sequence of said polynucleotide by hybridizing with a probe; a pharmaceutical composition comprising an effective amount of said polypeptide; a method for treating a disease or condition associated with decreased expression of functional HRIP, comprising administering to a patient said pharmaceutical composition; a method for screening a compound for effectiveness as an agonist or antagonist of said polypeptide; a method for screening a compound for effectiveness in altering expression of a polynucleotide sequence having the SEQ ID NO: 15;

2. Claims: 1-17, 20, 23 partially

Invention 2

Idem as subject 1 but limited to SEQ ID NOS: 2 and 16;

3.-14. Claims: 1-17, 20, 23 partially

Inventions 3-14

Idem as subject 1 but limited to SEQ ID NOS: 3-14 and 17-28.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 18, 19, 21 and 22

Claims 18, 19, 21 and 22 refer to an agonist and an antagonist of a polypeptide of claim 1 without giving a true technical characterization. Moreover, no such compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT).
No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the result to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/07277

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9839446 A	11-09-1998	AU 6545398 A	22-09-1998
		EP 0972029 A	19-01-2000
		EP 0972030 A	19-01-2000
		WO 9839448 A	11-09-1998
WO 9901541 A	14-01-1999	AU 726294 B	02-11-2000
		AU 8283698 A	25-01-1999
		EP 1005539 A	07-06-2000
WO 9900507 A	07-01-1999	US 5955338 A	21-09-1999
		AU 8269998 A	19-01-1999
		EP 0996733 A	03-05-2000

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: DIANA HAMLET-COX
INCYTE PHARMACEUTICALS, INC.
3160 PORTER DRIVE
PALO ALTO, CALIFORNIA 94304

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)*	04 OCT 2001

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
PF-0683 PCT	

International application No.	International filing date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/US00/07277	17 MARCH 2000	18 MARCH 1999

Applicant
INCYTE PHARMACEUTICALS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	REBECCA PROUTY for Barbara Badgero
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/IPEA/416 (July 1992)★

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PF-0683 PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/07277	International filing date *(day/month/year)* 17 MARCH 2000	Priority date *(day/month/year)* 18 MARCH 1999
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant INCYTE PHARMACEUTICALS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06 OCTOBER 2000	23 AUGUST 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Jaime Bridgers for REBECCA PROUTY Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/07277

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-67, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the claims:
pages 68-70, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/07277

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 18, 19, 21, AND 22

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 18, 19, 21, AND 22.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	2, 4, 10, 23	YES
	Claims	1, 3, 5-9, 11-17, 20	NO
Inventive Step (IS)	Claims	2, 4, 10, 23	YES
	Claims	1, 3, 5-9, 11-17, 20	NO
Industrial Applicability (IA)	Claims	1-17, 20, 23	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

All of Claims 1-17, 20 and 23 have been examined only with respect to SEQ ID NO:1 and its corresponding gene SEQ ID NO:15 as the Chapter I search was conducted only for this species.

Claims 1, 3, 5-9, 11-17, and 20 lack novelty under PCT Article 33(2) as being anticipated by Human Genome Sciences (WO98/39466).

Human Genome Sciences teach a human nucleic acid enoding a human protein having the nucleotide sequence disclosed in GCG GENESEQ database accession number V59579 which encodes a portion of SEQ ID NO:15 comprising residues 1362-2192 encoding residues 410-482 of SEQ ID NO:1. They teach host cells and transgenic organisms encoding this nucleic acid, expression of the encoded protein, antibodies to the encoded protein, methods of using the nucleic acid to isolate the complete gene, methods of screening for agonists and antagonists, pharmaceutical compositions and uses thereof.

Claims 1, 3, 5-9, 17, and 20 lack novelty under PCT Article 33(2) as being anticipated by Groom et al.

Groom teach a human nucleic acid encoding human Pyst1 and Pyst2 which each comprise an amino acid sequence comprising an immunogenic fragment of SEQ ID NO:1, host cells comprising these nucleic acids, expression of the encoded protein and assays for modulators of the activity of these proteins.

Claims 2, 4, 10 and 23 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a nucleic acid encoding SEQ ID NO:1.

---------- NEW CITATIONS ----------

NONE

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to adequately enable practice of the claimed invention because:

Claims 1, 5-17 and 20 are so broad as to encompass any polypeptide comprising an immunogenic fragment of SEQ ID NO:1 or polynucleotide encoding therefore. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides and polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of the polypeptide of SEQ ID NO:1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The description does not support the broad scope of the claims which encompass all modifications of any serine carboxypeptidase gene because the description does not establish: (A) regions of the protein structure which may be modified without effecting phosphatase activity; (B) the general tolerance of phosphatases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any peptidase residues with an expectation of obtaining the desired biological function; and (D) the description provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the (Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12N 9/16, 15/55, 1/21, 5/10, 15/11; C07K 16/40; C12Q 1/68, 1/42; A61K 38/46 and US Cl.: 435/196, 6, 21, 252.3, 325, 320.1; 536/23.1, 23.2; 424/94.6; 530/387.9

VIII. CERTAIN OBSERVATIONS ON THE APPLICATION (Continued):

claims broadly including genes encoding any number of amino acid modifications of the disclosed human phosphatase. The scope of the claims must bear a reasonable correlation with the scope of enablement. Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Claims 1, 3, 5-17 and 20 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
PF-0683 PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 00/07277	17/03/2000	18/03/1999
Applicant		
INCYTE PHARMACEUTICALS, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report.**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [X] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [X] furnished subsequently to this Authority in computer readble form.

   [X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [X] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   HUMAN REGULATORS OF INTRACELLULAR PHOSPHORYLATION

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

tional application No.
PCT/US 00/07277

Box I Observations where certain claims were found unsearchabl (Continuation of it m 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 16 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: 18, 19, 21 and 22
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-17, 20, 23 partially

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.